Review of: "Somatostatin and the pathophysiology of Alzheimer’s disease"

Juan Beauquis[1]

1 University of Buenos Aires

Potential competing interests: No potential competing interests to declare.

In this manuscript, Dr Almeida reviews evidence regarding the potential association of deficits found in somatostatin+ interneurons (SST-INs) with Alzheimer's disease (AD) pathogenesis and progression. The author proposes that when these GABAergic inhibitory interneurons are affected they lead to an excitatory/inhbitory imbalance in association with the promotion of amyloid deposition that would initiate AD. Somatostatin, co-secreted with GABA, has the capacity to aggregate and form mixed deposits of SST and amyloid in the brain parenchima, originating senile plaques. These aggregates would promote INs death and subsequent disinhibition of target neurons. This scenario would interfere with cognition, destabilizing older memories and precluding the formation of new memories.

I believe this is an interesting theoretical review, focusing on an alternative hypothesis for AD pathogenesis. Overall, the manuscript is well-written. I have some suggestions to improve the quality of this manuscript:

1. There is a slight lack of coherence between the abstract and the organization of the manuscript. The abstract points mostly to the potential pathophysiological process that affects SST-INs while there is only a brief mention to functional/cognitive deficits, which then are thoroughly reviewed through the manuscript. I would suggest to broaden the abstract in order to cover in a more balanced way the content of the review. I believe this would help potential readers to know what to expect from the review.
2. Regarding the conclusion/discussion of the review, I suggest to include a brief discussion or the author's point of view regarding how this model is in accordance or not with some of the most accepted AD hypotheses (e.g. amyloid cascade, metabolic, vascular, etc.). In my opinion, after a very thorough and extended review of the literature, a 'weighed’ summary of it would be very valuable.
3. Many of the references are cited without detailing if they refer to animal models, patients, in vitro evidence, etc. A more detailed description of the available scientific evidence would be important. Also, more information regarding which AD mouse model is cited in each case would improve the quality of the review.
4. When a group of references are cited together, many of them are repeated. Please check and correct this.
5. A grammar and typos check would greatly improve the manuscript.